

Cardiovascular Risk Reduction in the Workforce: Optimizing Cholesterol Management to Reduce the Burden of Cardiovascular Disease

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Cardiovascular disease (CVD) is among the most common health concerns in the United States and the costliest chronic condition. Cardiovascular disease includes hypertension, hyperlipidemia, heart failure, stroke, and coronary heart disease.¹ In 2008, CVD total costs were estimated at \$448.5 billion, and the predicted total cost for 2009 is \$475.3 billion.² Included in the projected total cost of CVD for 2009 are indirect costs totaling \$161.5 billion.² Indirect costs include morbidity, mortality, and lost productivity.² The most costly individual cardiovascular clinical events can include heart attack, stroke, and revascularization procedures.² Cardiovascular disease affects all age groups and races, and both women and men.² The economic impact of CVD on employers can be measured in both direct health-care costs and indirect costs (absenteeism, lost productivity) that negatively impact the fiscal bottom line.³

There is growing appreciation among health plan sponsors such as large employers that the financial impact associated with employees' health goes beyond direct medical expenditures.⁴ As this broader view of investment in health is accepted by occupational medicine and health benefit managers in general, programs that focus on the prevention of cardiovascular events will be adopted.⁴ Strategies for preventing complications due to CVD can typically include improving diagnosis, prompt initiation and optimization of treatment, and achieving quality measures. Programs that encourage individuals to follow recommended treatment strategies over long periods of time are gaining acceptance.⁵ These programs can help patients remain compliant with their clinicians' recommendations and prevent discontinuation of therapy.

REDUCING CVD RISK

Identifying risk factors for CVD has been the subject of intense clinical research for decades. Utilization of this

ABSTRACT

Cardiovascular disease (CVD), the leading cause of death in the United States, is at the forefront of our healthcare crisis, accounting for roughly one-sixth of the \$2.3-trillion healthcare expenditures in 2007. Available evidence suggests that diagnosis and treatment of this preventable condition is suboptimal. Effective screening, risk reduction, and disease management strategies—many of which can be implemented at the patient level—can curtail the morbidity and mortality of CVD and related expenditures, resulting in greater value for the individuals' health status. Short-term cost-containment strategies such as therapeutic substitution and increased patient cost sharing for prescription drugs may lead to decreased utilization and potentially increase unintended clinical outcomes and overall expenditures. Investment in prevention and treatment of CVD must consider overall effect on employee health and productivity, not exclusively direct health coverage costs.

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PRACTICAL IMPLICATIONS

Cardiovascular disease (CVD), the leading cause of death in the United States, is at the forefront of our healthcare crisis, accounting for roughly one-sixth of the \$2.3 trillion in healthcare expenditures in 2007.

- Effective screening, risk reduction, and disease management strategies—many of which can be implemented at the patient level—can curtail the impact of CVD and related expenditures, resulting in greater value for individuals' health status.
- Short-term cost-containment strategies such as therapeutic substitution and increased patient copayments for prescription drugs may lead to decreased utilization and potentially increase unintended clinical outcomes and overall expenditures.
- Investment(s) in prevention and treatment of CVD must consider overall effects on employee health and productivity, not exclusively direct medical costs.

knowledge by clinicians and individuals has been sub-optimal, representing an enormous public health opportunity.⁵ The American College of Cardiology/American Heart Association Task Force on Performance Measures, which provides leadership in enhancing the quality of cardiovascular care, believes that compliance with their measures encourages the strongest evidence-based care (for more information on the databases and search terms used to develop this manuscript, see the [eAppendix](#) available at www.ajpbllive.com). From both a public and an individual perspective, identifying and reducing risk factors for adverse events have become major objectives for clinicians using evidence-based care to achieve better patient outcomes.⁵ Key risk factors include nonmodifiable risk factors such as family history of CVD and age (men >45 years, women >55 years), and modifiable risk factors including hypertension, high low-density lipoprotein cholesterol (LDL-C), low high-density lipoprotein cholesterol (HDL-C), smoking, obesity, physical inactivity, and diabetes.^{6,7} Through a variety of programs, employers can play a critical role in executing an effective and efficient CVD prevention strategy aligned with the organization's clinical and business goals.⁸

Role of Cholesterol Management in Reducing the Risk of CVD

Addressing each of the modifiable risk factors for CVD is beyond the scope of this article. Our objective in this commentary is to focus on the detection and

management of hypercholesterolemia or elevated cholesterol where there is a clearly identified opportunity for optimization of therapy to reduce CVD burden. Screening for hypercholesterolemia, which can be performed easily at the worksite, has been identified by the Centers for Disease Control and Prevention (CDC) as a cost-effective preventive service.⁸ The Adult Treatment Panel III includes total cholesterol, LDL-C, HDL-C, triglycerides (TGs), and very low-density lipoprotein in cholesterol screening.⁶ High-density lipoprotein cholesterol protects against the development of CVD, as it is responsible for bringing cholesterol to the liver so that it can be removed from the body.^{6,7} High levels of HDL-C are associated with a reduced risk of stroke or cardiovascular events.^{6,7} Low-density lipoprotein cholesterol is a risk factor for the development of CVD, as it carries cholesterol in the bloodstream from the liver to other parts of the body.^{6,7} Low-density lipoprotein cholesterol is the primary target of lipid-lowering therapy, and elevated levels prompt the initiation and intensification of treatment.^{6,7} Triglycerides are the primary source of fat used by the body for energy storage, and increased levels increase cardiovascular risk when coupled with high LDL-C levels.⁶ Elevated levels of TG often are associated with diabetes mellitus.⁶ Very low-density lipoprotein is responsible for the distribution of TG, and high levels contribute to heart disease and stroke risk.^{6,7}

For patients with 1 or fewer risk factor for CVD, the LDL-C goal is less than 160 mg/dL.⁷ For patients with 2 or more risk factors for CVD, the LDL goal is less than 130 mg/dL.⁷ For patients with established CVD or a CVD risk equivalent such as diabetes, the LDL goal is less than 100 mg/dL.⁷ The updated 2004 National Cholesterol Education Program (NCEP) guidelines provide LDL-C goals for high-risk patients with clinically evident CVD.^{7,9} For very high-risk patients, a target LDL-C of less than 70 mg/dL is considered optional for some patients with lower baseline LDL-C.^{8,9}

When hypercholesterolemia is detected, NCEP guidelines suggest that management of hypercholesterolemia greatly reduces heart disease risk.⁶ Risk prevention is classified into either primary or secondary prevention. Primary prevention focuses on decreasing the burden of CVD by addressing modifiable risk factors (eg, diet, exercise) to avoid the occurrence of the disease.⁹ This focus has been recently expanded to include more stringent LDL-C goals as a means of primary prevention for individuals with an estimated CVD risk of greater than 20% over 10 years, or for patients with diabetes.⁹ Secondary prevention focuses on slowing progression of an already

diagnosed disease state.¹⁰ Secondary prevention includes treatment of hypercholesterolemia after a patient has had a heart attack or CVD is confirmed by angiography.¹⁰

Nondrug Interventions

Nondrug interventions are the first-line intervention for most patients with CVD and for those who are at risk for CVD.⁶ The cornerstones of nonpharmacologic interventions are smoking cessation, diet and exercise modifications or Therapeutic Lifestyle Changes (TLC), and reduction in alcohol consumption.^{6,7} As part of TLC, patients with LDL-C above 130 mg/dL should limit intake of saturated fat to less than 7% of daily calories, limit fat intake to less than 25% to 35% of total calories, limit sodium intake to less than 2400 mg, and limit cholesterol to less than 200 mg/day.⁶ Carbohydrates should generally account for 50% to 60% of total calories, and protein should account for 15% of total calories.⁶ The total calories that make up the diet are individualized through collaboration with the patient's healthcare provider.⁶ The TLC diet also should include 2 g of plant stanols/sterols per day and 10 to 25 g of soluble fiber per day.⁶ The NCEP guidelines recommend at least 30 minutes of moderate-intensity physical activity most days of the week.⁶ An effective TLC program can potentially decrease total cholesterol by 25% to 30% and have a beneficial impact on LDL-C, HDL-C, TG, and weight.⁷

Pharmaceutical Interventions

There are numerous pharmacologic options for primary and secondary prevention of CVD. HMG-CoA reductase inhibitors (statins) are the most potent, widely used, and effective agents for reducing LDL-C and to a lesser extent raising HDL-C and lowering TG. Statins can potentially decrease LDL-C by 30% to 60%. Nicotinic acid or niacin and fibric acid derivatives are second-line agents primarily used for reducing TGs and increasing HDL-C with modest reduction in LDL-C. Fibrates and nicotinic acids become first line when TGs are very high. Nicotinic acid or niacin has an ability to reduce LDL-C, raise HDL-C, and decrease TG. Fibric acid derivatives lower LDL-C by 22% in lone LDL-C hypercholesterolemia and lower TG and raise HDL-C for mixed dyslipidemia. Bile acid sequestrants such as cholestyramine are other agents used to reduce LDL-C and modestly increase HDL-C, although they have no discernible effect on TG levels.^{6,7}

Statins. Statins are the cornerstone of CVD prevention and treatment programs, and are among the most commonly prescribed drug classes.^{11,12} According to what science tells us, summarized by the US Department of

Table. Statins and Generic Availability^a

Drug Name	US Market Manufacturer	Generic Available?
Atorvastatin (Lipitor)	Pfizer	No
Fluvastatin (Lescol)	Novartis	No
Lovastatin (Mevacor)	Merck	Yes
Pravastatin (Pravachol)	Bristol-Myers Squibb	Yes
Rosuvastatin (Crestor)	AstraZeneca	No
Simvastatin (Zocor)	Merck	Yes

^aSources: Lipitor (atorvastatin) [package insert]. New York, NY: Pfizer; revised March 2007; Lescol (fluvastatin) [package insert]. Kenilworth, NJ: Novartis Pharmaceuticals Corporation; revised October 2006; Mevacor (lovastatin) [package insert]. Whitehouse Station, NJ: Merck Research Laboratories; 2007; Pravachol [package insert]. Princeton, NJ: Bristol-Myers Squibb; 2007; Crestor [package insert]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; 2007; Zocor [package insert]. Whitehouse Station, NJ: Merck Research Laboratories; revised June 2008.

Health and Human Services and the CDC, statins are effective at reducing mortality from heart disease through their cholesterol-lowering actions.^{12,13} Although these agents often are discussed as interchangeable, the fact remains that not all statins are the same, nor do they all have a generic equivalent product at this time (Table). According to generally accepted medical or pharmacy practice standards, consideration must be given to proven heart disease outcomes, safety profile, US Food and Drug Administration–approved indications, risk reduction across individual patients, years of clinical experience, and effective lipid lowering to attain treatment goals when choosing among available statins. One or more conclusions may be reached as a result of those product review considerations, as in any therapeutic category where substitution may be considered (Table).

IMPORTANCE OF MEDICATION TREATMENT ADHERENCE TO ACHIEVE DESIRED CLINICAL AND ECONOMIC OUTCOMES

Despite the extensive use of statins, only a portion of employees with elevated cholesterol may have this condition detected or receive treatment. Moreover, those prescribed therapy may discontinue the medication and those who have taken the prescribed regimen religiously may not achieve LDL-C goals.¹⁴

In a sample of 4148 men and women from the 1999–2004 National Health and Nutrition Examination Survey,

the mean total cholesterol was calculated as 203 mg/dL. For participants with hypercholesterolemia, defined as total cholesterol greater than 200 mg/dL or active treatment for hypercholesterolemia, only 69.5% reported having cholesterol screening prior to the study. Only 35.0% of the same population knew they had hypercholesterolemia. Remarkably, only 12.0% were in the healthcare system and being treated for hypercholesterolemia. Regrettably, only 5.4% had achieved treatment goal or a total cholesterol level of less than 200 mg/dL. These data clearly show that patients are not being adequately screened for hypercholesterolemia, and when treatment is initiated there is inadequate follow-up, including appropriate therapy intensification. Given the robust data presented in the 2000 NCEP II guidelines and more aggressive LDL goals in subsequent NCEP III guidelines, the US health system needs to renew its efforts to manage cholesterol and lower total cholesterol in the United States.¹⁵

Role of Benefit Design to Optimize CVD Investment

Interventions aimed at keeping individuals with elevated cholesterol on therapy, with regular assessment of whether appropriate agents and dosages are used, are paramount for plan sponsors to optimally manage heart disease risk and maximize their return on investment on the dollars spent to reduce the burden of CVD. Investment value considerations may vary among different types of plan sponsors such as self-funded unions, employers, municipalities, or fully insured health plans.

To achieve the benefits of a CVD prevention/treatment program, incentives in benefit design should be aligned with overall business strategy and goals. A more frequent component of pharmacy benefit strategy has been to implement various tactics such as multitiered formularies, step edits, and increased patient copayments to reduce short-term spending on drugs.¹⁶ Other strategies have included using other out-of-pocket programs with various deductible or coinsurance amounts, or combinations that include varied copayments. These programs, however, may adversely impact medical direct costs for the patient and plan sponsor, as well as other indirect costs borne by plan sponsors such as employers, because of increased absence or reduced productivity associated with diminished health.

Drug Substitution Programs

Distinguishing between generic and therapeutic substitution is an important consideration for benefit managers when considering the clinical and fiscal effects of these substitution or switch programs. *Generic substitution* is a practice whereby the pharmacist substitutes the

exact chemical entity (as either an unbranded drug or different brand name) for the brand originally prescribed by the physician.¹⁷ Thus, in a generic substitution program, the same chemical compound in the same dosage form is provided, usually from a different manufacturer. *Therapeutic substitution* refers to replacing the drug originally prescribed by the physician with a *different chemical entity*. This results in a different drug from the same therapeutic category being substituted.¹⁷ A careful review of the scientific evidence—in addition to cost considerations—should be a key component in making benefit design coverage decisions regarding therapeutic substitution because individual patients may respond or adhere differently to a new chemical entity.¹⁸

Increases in Patient Out-of-Pocket Costs

Any intervention program that alters factors in the clinical management of patients has intended and unintended consequences. Therapeutic switching programs are not the only intervention impacting a high-value pharmaceutical class such as statins. Copayments have been the most common and visible component of benefit programs that consumers pay at the point of care, although coinsurance and deductible amounts also are used, and all have risen in recent years for prescription drug programs. For one example, from 2000 to 2007 the average copayment for generic drugs, preferred branded drugs, and nonpreferred branded drugs increased by 38%, 67%, and 48%, respectively.¹⁹

Owing to the focused and longer-term use of statins within a benefit design, longitudinal studies have demonstrated that patient compliance with these agents is negatively impacted by increases in patient copayments.^{19,20} Although across-the-board increases in copayments may be justified as a response to cost pressures, it is difficult to defend such an unintended effect of raising copayments. Use of statins for the management of elevated cholesterol is considered to be an indicator of high-quality care.²¹

Advocates of value-based insurance design (VBID) argue for a “clinically sensitive” cost-sharing system that reflects clinical benefit and cost-effectiveness of interventions.²² The basic VBID premise is that patient contributions for high-value services remain low. For example, patient copayments for high-value drug classes (statins, beta-blockers, hypoglycemics, and asthma controllers) should be lower—within the existing tiered formulary system—than those considered to be of less value. This design has been successfully implemented by several large employers and health plans.^{22,23}

Over the long term, it is possible that nonadherence to therapy can lead to increased overall healthcare costs and hospitalization risk.²⁴ The clinical implications depend on the extent to which patients, when faced with higher branded copayments, shift to generic alternatives (if available) or discontinue use entirely.

The debate pertaining to the relative merits of branded and generic statins or other drug categories is beyond the scope of this commentary. However, it may be clinically desirable to have a variety of branded and generic agents within a class because of heterogeneity in patient responses to treatment (eg, allergy, drug interaction, adverse effect, lack of desired clinical effect). For these situations, the cost-sharing method(s) used for the preferred or brand drug(s) in high-value classes should be lowered after an unsuccessful trial with an available generic option. This “reward the good soldier” approach maintains financial incentives to use generics initially, but mitigates concern that patients who do not respond to generics would discontinue high-value medications altogether due to the additional financial burden associated with brand-name drugs, particularly in a recessionary economic period. This concept differs from step-edit or “fail first” programs in that in the good soldier paradigm, patient copayments are lowered for branded drugs once appropriate usage is determined, as opposed to existing programs that keep copayments unchanged.

Given concerns about healthcare expenditures and medical loss ratios, it is reasonable for at-risk plan sponsors to reevaluate broad therapeutic substitution programs. Although short-term drug savings may be achieved, a switch program that results in poor adherence or complete discontinuation may have cost and productivity implications for both the employee patient and the plan sponsor payer—in addition to the administrative burden on clinician or pharmacy network providers.¹⁸

BENEFIT DESIGN: QUESTIONS AND CONSIDERATIONS

The provider community can assist plan sponsors in sorting through benefit coverage considerations so that they can simultaneously manage CVD risk and address the fiscal bottom line. Examples of multistakeholder questions that warrant consideration regarding healthcare benefits may include the following:

- What does benefit coverage for managing CVD risk mean to employees as members of the health plan?
- Are risk factors identified (ie, health status assessment, biometric testing)?

- Are there existing barriers to recommended screening tests?
- How effectively are employees or families being treated for CVD risk?
- How does the current formulary provide incentives or disincentives to employees to remain adherent to recommended drug classes of high clinical value?
- Will a difference in patient copayments for brand and generic statins lead to patient discontinuation if their clinician feels a branded product is necessary?

Benefit design considerations for health plans or pharmacy benefit managers may include the following:

- Can health and disease management programs such as screening and monitoring be implemented and/or maximized along with aligning incentives for maintenance drug use?
- Is the current formulary and benefit design working, or should a different model that may align better with coverage goals be considered?
- How could the employer work more effectively with health plans, physicians across the community, and pharmacy benefit managers on medication coverage issues?

SUMMARY

Diagnosis and management of heart disease risk are important clinical and fiscal issues to patients as well as to health plan sponsors (eg, employers, unions). The impact of these issues extends far beyond medical expenditures. Modifiable risk factors for CVD are the focus of quality improvement initiatives and health benefit coverage. As CVD is the most common and costly medical condition that impacts all patient groups as well as plan sponsor types, continued risk factor identification and evidence-based management, including use of nonpharmaceutical interventions and drugs (most notably statins and aspirin, when appropriate), can lead to improvements in medical and fiscal results.

Greater efforts must be made by all healthcare stakeholders to improve upon suboptimal long-term adherence rates for evidence-based therapies. Interventions aimed at reducing healthcare expenditures such as therapeutic change programs or increases in patient out-of-pocket costs can cause unintended consequences such as interruption or reduction in the use of drugs, unwanted clinical adverse events, and negative cost and productivity implications for the employer. These are areas for future research and study.

Clinicians and payers must be increasingly sensitive to the trade-offs between access to care and cost-containment programs, as these directly impact not only the healthcare status of their patients, but cost as well. Management of CVD in accordance with evidence-based guidelines is one crucial step in the disease management process, one that, coupled with successful benefit-innovation strategies, can streamline healthcare spending while ensuring delivery of the most value-based and appropriate medical care for employees/patients.

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eAppendix. Databases and Search Terms^a

Databases Searched	Search Terms
American Academy of Pediatrics	Generic substitution Therapeutic substitution
American Heart Association	Cholesterol CVD costs CVD statistics Statin
Centers for Disease Control and Prevention	CVD costs CVD statistics
Medscape	Cholesterol CVD costs Fibrate Statins TLC diet
Micromedex	Lescol Lipitor Lovastatin Pravachol Zocor
National Heart, Lung, and Blood Institute	ATP III Cholesterol guidelines NCEP
National Institutes of Health	ATP III NCEP guidelines

ATP III indicates Third Report of the Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III); CVD, cardiovascular disease; NCEP, National Cholesterol Education Program; TLC, Therapeutic Lifestyle Changes.

^aNo advanced terms (eg, years, dates) were used when searching the databases.